Eya1 protein phosphatase regulates tight junction formation in lung distal epithelium.

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Public Summary:
Little is known about the regulatory mechanisms underlying lung epithelial tight junction (TJ) assembly, which is inextricably linked to the preservation of epithelial polarity, and is highly coordinated by proteins that regulate epithelial cell polarity such as aPKCζ. We recently reported that Eya1 phosphatase functions through aPKCζ-Notch1 signaling to control cell polarity in the lung epithelium. Here, we have extended these observations to TJ formation to demonstrate that Eya1 is crucial for the maintenance of TJ protein assembly in the lung epithelium, probably by controlling aPKCζ phosphorylation levels, aPKCζ-mediated TJ protein phosphorylation and Notch1-Cdc42 activity. Thus, TJs are disassembled after interfering with Eya1 function in vivo or during calcium-induced TJ assembly in vitro. These effects are reversed by reintroduction of wildtype Eya1 or partially inhibiting aPKCζ in Eya1siRNA cells. Moreover, genetic activation of Notch1 rescues Eya1(-/-) lung epithelial TJ defects. These findings uncover novel functions for Eya1-aPKCζ-Notch1-Cdc42 as a crucial regulatory mechanism of TJ assembly and polarity of the lung epithelium, providing a conceptual framework for future mechanistic and translational studies in this area.

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